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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/917,897 | 07/31/2001 | Masashi Ogawa | Q65704 | 2025 |

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EXAMINER

MORAN, MARJORIE A

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| ART UNIT | PAPER NUMBER |
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1631

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.A.M.

Office Action Summary**Application No.**

09/917,897

Applicant(s)

OGAWA ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3 and 5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3 and 5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 09/125,944.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/22/03 has been entered. All rejections and objections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant's arguments with respect to claims 3 and 5 have been considered but are moot in view of the new ground(s) of rejection.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over SALTHOUSE et al. (Experientia (1970) vol. 26 (2), pp. 220-221) in view of GALIS et al. (FASEB (7/1995), volume 9, pages 974-980) and BATTISTA (US 3,649,347).

Claim 3 recites a method of detecting a protease in a biological sample by contacting one of multiple continuous slices of the sample with a thin membrane comprising a protease substrate and a hardener on a support, contacting the remaining slices of the sample with a similar thin membrane which also comprises a protease inhibitor, detecting traces of digestion on the membranes, and comparing the two.

SALTHOUSE teaches a method for detecting protease in a sample wherein tissue sections are contacted with a dried thin membrane comprising collagen cross-linked on a support, and comparing digestion of the collagen to digestion of collagen soaked in a protease inhibitor (p. 221). SALTHOUSE does not specifically teach cross-linking agents nor sections which are "substantially continuous".

GALIS teaches a method of detecting a protease in a biological sample wherein consecutive sections of the sample are brought into contact with a thin membrane comprising a support holding a fluorescent substrate mixed with a protease substrate, and other sections are brought into contact with similar thin membranes with protease

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inhibitors incorporated, and the results from the two are compared (p. 975: Protocol and Controls).

BATTISTA teaches a variety of cross-linkers for collagen and teaches that cross-linking may improve the properties of thin films comprising the collagen (col. 6, lines 29-50). BATTISTA specifically teaches that his cross-linked collagen may successfully be applied to a variety of supports, including glass and films (col. 5, lines 10-29).

It would have been obvious to one of ordinary skill in the art at the time of invention to have contacted the slides of SALTHOUSE in the method of SALTHOUSE with consecutive sections of sample, as taught by GALIS, where the motivation would have been to assay for enzyme activity across a series of tissue slices, as taught by the method of GALIS and suggested by the cryostat slices and tissue sections of SALTHOUSE. It would further have been obvious to have added the cross-linking agents of BATTISTA to the collagen on the supports/slides in the method of SALTHOUSE where the motivation would have been to improve the properties of the collagen, as taught by BATTISTA. One skilled in the art would reasonably have expected success in incorporating the cross-linkers of BATTISTA with the collagen in the method of SALTHOUSE because BATTISTA teaches that his cross-linked collagen may successfully be used on a variety of surfaces and for a variety of purposes, as set forth above.

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Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over SALTHOUSE et al. (Experientia (1970) vol. 26 (2), pp. 220-221) in view of BATTISTA (US 3,649,347) and LAWRENCE et al. (IDS ref: US 5,416,003).

Claim 5 recites a method wherein a sample (not limited to be slices) is contacted by a thin membrane comprising layers laminated together on a support, wherein one layer comprises a protease substrate and a hardener, and a second layer comprises a substrate, hardener, and inhibitor, and the traces of digestion on the two layers are detected and compared.

SALTHOUSE teaches a method for detecting protease in a sample wherein tissue sections are contacted with a dried thin membrane comprising collagen cross-linked on a support, and comparing digestion of the collagen to digestion of collagen soaked in a protease inhibitor (p. 221). SALTHOUSE does not specifically teach cross-linking agents nor a multiply layered film.

BATTISTA teaches a variety of cross-linkers for collagen and teaches that cross-linking may improve the properties of thin films comprising the collagen (col. 6, lines 29-50). BATTISTA specifically teaches that his cross-linked collagen may successfully be applied to a variety of supports, including glass and films (col. 5, lines 10-29), and teaches that his collagen may be used on multiply layered substrates (col. 5, lines 30-40).

LAWRENCE teaches a device for detecting proteases in samples wherein multiple layers are laminated together, and wherein one layer may comprise a substrate

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and another layer may comprise an inhibitor (col. 23, lines 55-62 and col. 24, lines 34-39).

It would have been obvious to one of ordinary skill in the art at the time of invention to have laminated a layer comprising a substrate, hardener, and inhibitor to a layer comprising a substrate, hardener, and inhibitor in a multilayer analytical element, as taught by LAWRENCE, for use in the method of SALTHOUSE where the motivation would have been to facilitate measurement of protease in a single sample using a single test element, as suggested by the teaching of LAWRENCE that a test element comprising laminated layers can be used to detect proteases. It would further have been obvious to have used included any of the crosslinkers BATTISTA in a multiply layered test element in the method made obvious by SALTHOUSE and LAWRENCE where the motivation would have been to improve the properties of the collagen, as taught by BATTISTA. One skilled in the art would reasonably have expected success in incorporating the cross-linkers of BATTISTA with collagen in a multiply-layered element for use in a method to detect proteases because BATTISTA teaches that his cross-linked collagen may successfully be used in multiply-layered elements, LAWRENCE teaches that multiply-layered elements may be used to detect proteases, and SALTHOUSE teaches that collagen can be used to detect proteases.

Conclusion

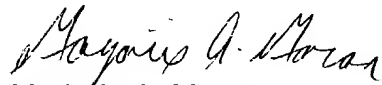
Claims 3 and 5 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon. to Wed, 7:30-4; Thurs 7:30-6; Fri 7-1 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Marjorie A. Moran
Primary Examiner
Art Unit 1631

mam